Comparison of diagnostic performance of transesophageal echocardiography and positron emission tomography in patients with cardiovascular implantable electronic device infections

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ABSTRACT

Background: The modified Duke criteria and transesophageal echocardiography (TEE) are often insufficient to diagnose infective endocarditis in patients with cardiovascular implantable electronic devices (CIEDs). F-18-fluoro-2-deoxy-glucose positron emission tomography (18F-FDG PET/CT) is a promising method for detecting lead endocarditis.

Aims: The study aimed to compare diagnostic performance of 18F-FDG PET/CT and TEE in detecting lead endocarditis (LE).

Methods: We included 40 patients admitted to the hospital for CIED infection. Patients were classified as "LE-positive" and "LE-negative" according to TEE and 18F-FDG PET/CT findings. After three months of follow-up, the patients' lead cultures, tissue and blood cultures, and clinical responses after antibiotic treatment were reviewed using the Duke criteria. The final exact diagnosis was compared with 18F-FDG PET/CT and TEE findings.

Results: No involvement was observed on 18F-FDG PET/CT in 12 patients (30%). The remaining 25% of patients had device pocket involvement, and two patients had systemic involvement. In the follow-up of 23 patients diagnosed with LE by TEE, 14 were consistent with LE. Seventeen of 18 patients with suspicion of LE were diagnosed with definite LE by 18F-FDG PET/CT. Six of the 22 patients with negative 18F-FDG PET/CT scans were false negative and diagnosed as definite infective endocarditis. 18F-FDG PET/CT had sensitivity of 73.9% and specificity of 94.1%. It was observed that there was a statistically significant difference between TEE and PET ($P = 0.006$).

Conclusion: 18F-FDG PET/CT is superior to TEE in diagnosing IE in patients with CIED.

Key words: Cardiovascular implantable electronic devices, positron emission tomography, transesophageal echocardiography

INTRODUCTION

Infective endocarditis is a severe condition that results in significant morbidity and mortality [1]. Its incidence ranges from 3 to 10 cases per 100 000 annually and steadily increases. This rise is linked to the growing use of cardiac implantable electronic devices (CIED) and heart valve repair and replacement procedures, driven by increasing life expectancy in recent years [2].

Cardiovascular implantable electronic devices have recently been widely utilized to improve the quality of life and prolong the lifespan of heart disease patients [2]. Device-related infection is recognized as one of the most severe complications of CIED implantation. Providing an accurate incidence of CIED infections is challenging due to variations in disease definition, diversity of the patient population, and heterogeneity in

WHAT'S NEW?

Our study, the first to compare the performance of direct transesophageal echocardiography (TEE) and 18F-FDG PET/CT (F-18 fluoro-2-deoxy-glucose positron emission tomography) in diagnosing lead endocarditis in patients with cardiovascular implantable electronic devices, has significant implications for clinical practice. While no previous study has directly compared 18F-FDG PET/CT to TEE, earlier research demonstrated the superiority of 18F-FDG PET/CT in diagnosing lead endocarditis and pocket infections. Our study supports this by showing that 18F-FDG PET/CT is a superior imaging modality for diagnosing lead endocarditis compared to TEE. This is particularly relevant in cases where TEE struggles to distinguish thrombus, vegetation, or fibrosis on the lead, which makes 18F-FDG PET/CT a valuable additional imaging modality for vegetation discrimination. These results strongly advocate for the use of 18F-FDG PET/CT in cases where there is a suspicion of lead endocarditis, and TEE examination is insufficient.

patient numbers in the studies. Infections associated with CIEDs occur at a rate ranging from 1% to 7%, depending on the type and complexity of implantation [2, 3]. Previously published data showed that infection rates increased significantly from 1.45% to 3.41%, with cardiac resynchronization therapy with pacemaker/device experiencing the most significant increase [4]. The infection rate is highest shortly after surgery (in the first three months). Infections are known to cause increased morbidity and death, particularly in the case of systemic and delayed (3–12 months) localized infections [5].

Risk factors for infective endocarditis associated with CIED include younger age during implantation, male sex, diabetes mellitus, end-stage renal failure, previous history of device infection, malignancy, heart failure, chronic obstructive pulmonary disease, steroid use, and anticoagulant use [2, 6]. Also, procedure-related factors like postoperative hematoma, intervention following lead displacement, device replacement or revision, absence of antibiotic prophylaxis, temporary pacing, lack of adequate experience, prolonged procedure duration, an abdominal device pocket, epicardial leads, and the presence of two or more leads heighten the risk of infection [6–8].

Diagnosing CIED infections to ascertain whether the disease is confined to the device pocket or involves the leads and/or heart valves represents a significant challenge [9]. Currently, diagnosis of infective endocarditis (IE) relies on the modified Duke criteria, and additionally, an international diagnostic algorithm for evaluating infection introduced in 2019 to refine the diagnosis of CIED infections [6]. Transesophageal echocardiography (TEE) is often the preferred imaging method for assessing lead endocarditis. Nevertheless, TEE diagnosis should be interpreted with caution due to such challenges as distinguishing lead reflections and echoes, atypical vegetation localizations, and its difficulties in discerning vegetation and thrombus [10].

In recent years, single-photon emission computed tomography (SPECT/CT) and positron emission tomography (18F-FDG PET/CT) have emerged as promising tools for diagnosing endocarditis [11, 12]. These advanced imaging modalities offer significant advantages, particularly in conditions where the Duke criteria exhibit low sensitivity, such as prosthetic valve endocarditis and CIED infection. Notably, in diagnosing pocket infections, 18F-FDG PET/CT demonstrates impressive sensitivity and specificity of up to 93% [13].

This study aimed to evaluate and compare the diagnostic performance of 18F-FDG PET/CT and TEE in identifying lead endocarditis in patients with implantable cardiac electronic devices and suspicion of lead endocarditis due to pocket infection.

METHODS

Between 2014 and 2018, we studied patients who were referred to our hospital with a device pocket infection. All patients showed evidence of device pocket infection, and the investigation focused on whether or not they had lead endocarditis. The inclusion criteria were a device pocket infection diagnosis, availability of clinical and laboratory records, TEE and 18-FDG PET/CT data, and at least three months of clinical follow-up to confirm the diagnosis of endocarditis. The exclusion criteria were being under 18 years of age and IE being excluded based on the 18-FDG PET/CT or TEE results.

Between 2014 and 2018, around 78 patients presented in our hospital with a suspected device pocket infection and endocarditis. However, 18-FDG PET/CT scans were not available for 30 of these individuals. Between 2014 and 2016, eight of 18F-FDG PET/CT scans were performed. It was reported that the prevalence of 18F-FDG PET/CT imaging increased after 2016. Additionally, four patients were removed from analysis since their TEE images had been obtained from outside sources. The remaining four patients were discharged from our facility owing to treatment refusal and were unavailable for clinical follow-up. As a result, statistical analyses were done on 40 patients (Figure 1).

The medical records of all the patients were reviewed. Blood cultures, TEE, and PET/CT imaging findings were analyzed. All patients underwent both transthoracic echocardiography and TEE examinations. Transthoracic and transesophageal echocardiographic evaluations were performed using multifrequency transthoracic transducers ranging from 2.5 FPA to 1.5–3.6 MHz and 5 MHz multiplane

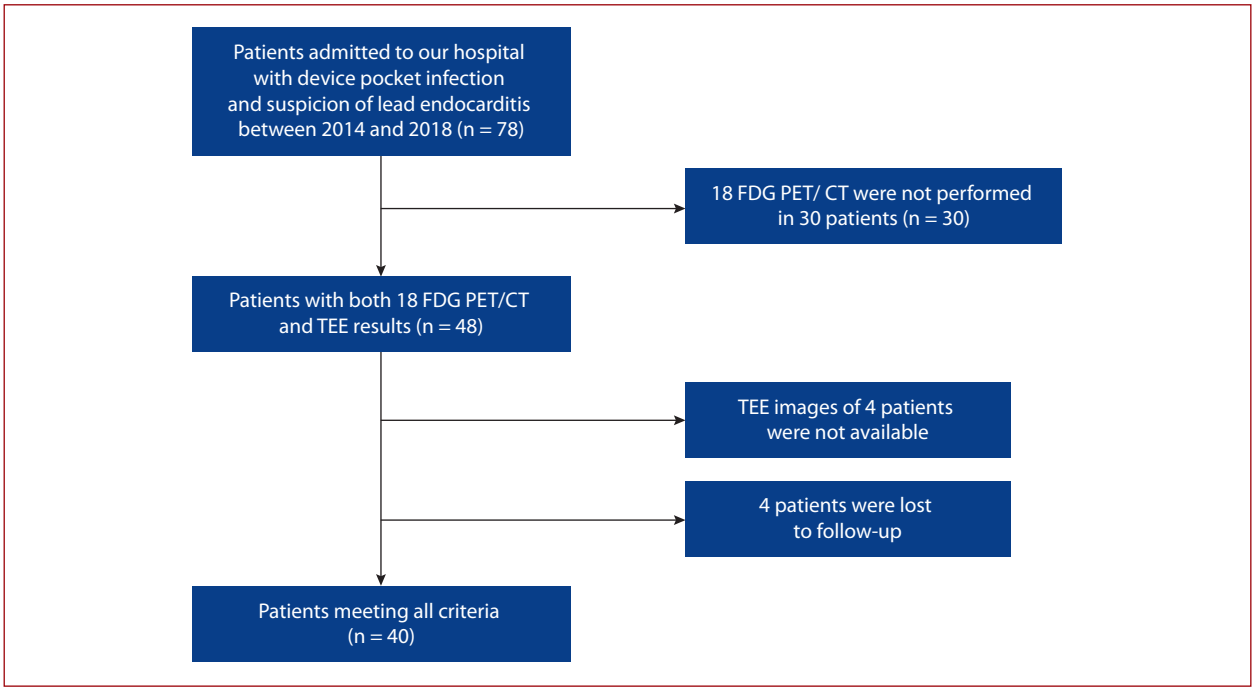

Figure 1. Patient flow

Abbreviations: TEE, transesophageal echocardiography; 18F-FDG PET/CT, F-18 fluoro-2-deoxy-glucose positron emission tomography

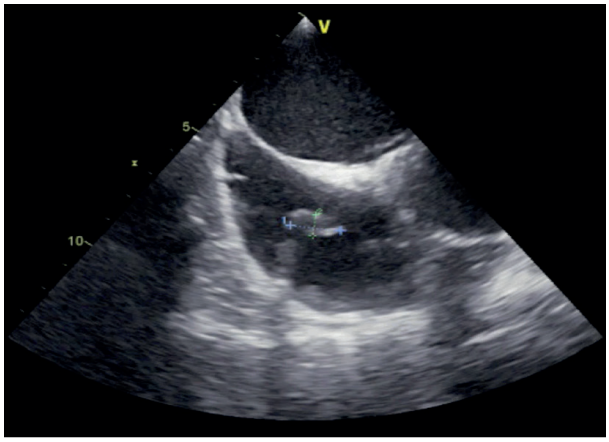

Figure 2. A fixed mass encircling the lead was observed on transesophageal echocardiography study

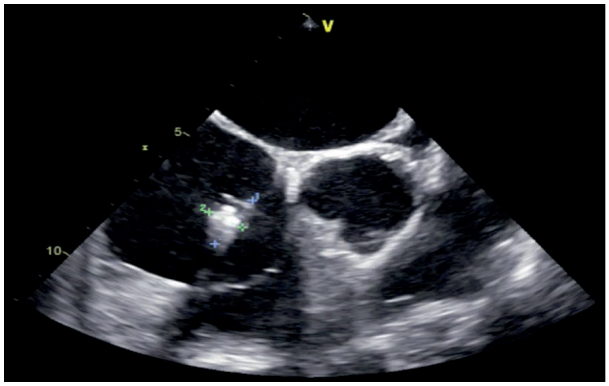

Figure 3. A mobile mass around the lead was observed on transesophageal echocardiography study

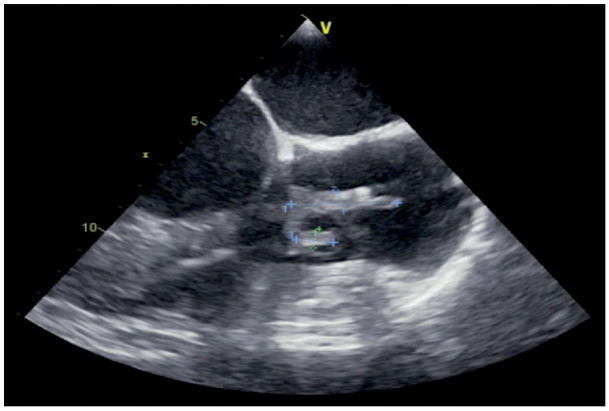

Figure 4. Multiple masses around the lead were observed on transesophageal echocardiography study

transesophageal transducers. The masses detected during TEE were classified based on their mobility and number: fixed masses were immobile encircled structures, causing thickening around the lead (Figure 2), while mobile masses were thin fibrillary structures attached to the lead (Figure 3), and the presence of multiple structures was termed as multiple masses (Figure 4).

All patients also underwent 18F-FDG PET/CT scans. These patients obtained approvals from three physicians and had a high clinical suspicion of endocarditis, which is required for 18F-FDG PET/CT scans in Türkiye. A positive diagnosis of CIED infection *via* 18F-FDG PET/CT was es-

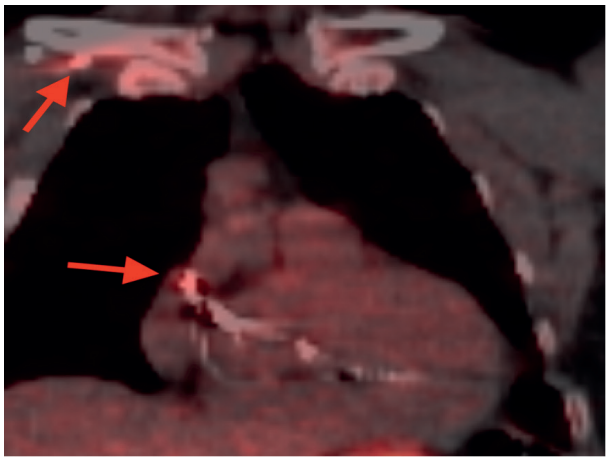

Figure 5. Positive PET/CT examination demonstrating uptake of 18-FDG by the leads

tablished in the presence of abnormally elevated 18F-FDG uptake localized in the pocket or leads. Based on the 18F-FDG PET/CT scan results, patients were allocated into two groups: with or without lead endocarditis (LE). An 18F-FDG uptake pattern suggestive of lead involvement (post-venous entry) and/or indicative of septic emboli or cardiac valve involvement was deemed a positive PET/CT result for lead endocarditis (Figure 5). Conversely, an increased 18F-FDG uptake confined to the CIED generator pocket without lead involvement was considered negative for lead endocarditis.

During pocket removal procedures, tissue samples were obtained and sent for culture. Lead extraction was performed according to the guidelines, and cultures of the intravascular segments of the extracted leads were conducted. Patients were classified as having pocket infection if we observed cellulitis affecting the pocket area, purulent discharge from the incision site (excluding uncomplicated suture abscess), wound dehiscence, erosion of the skin by the generator or electrodes, signs of abscess or fistula formation, or systemic symptoms/signs of systemic infection.

Diagnosis of lead endocarditis was based on the Duke criteria: "definite LE" if two major criteria or one major and three minor criteria, or five minor criteria were met; "possible LE" if one major and one minor criterion or three minor criteria were met; and "no LE" if these criteria were not met or an alternative diagnosis was made. Subsequently, patients' TEE and 18F-FDG PET/CT results were classified as "definite LE" or "no LE". Throughout the 3-month follow-up, the patient's blood, tissue, and lead culture results were monitored. We evaluated if patients received antibiotic treatment, their clinical symptoms, and biochemical analyses at specific intervals. Complete blood count, C-reactive protein, and sediment tests were performed weekly for inpatients and every 2 or 4 weeks for outpatients. We performed physical examinations (peripheral signs of endocarditis, appearance of the battery pocket, newly developed murmurs) and monitored symptoms (fever, fatigue, loss of appetite, muscle and joint pain). Findings were noted. We recorded deaths of patients who developed hemodynamic instability during follow-up. After 3 months of follow-up, all these results were reviewed according to the Duke criteria, and definitive diagnosis was made. This final diagnosis was then compared with the 18F-FDG PET/CT and TEE findings, providing a comprehensive overview of the patients' condition.

Ethics

This retrospective data analysis study did not require informed consent. The study protocol was approved by our center's local ethical committee (decree no: 02-123-19, date: 28/01/2019).

Statistical analysis

R Statistical software version 4.3.0 (R Foundation for Statistical Computing, Vienna, Austria) was used for statistical analyses. Descriptive statistics were presented as mean standard deviations for normally distributed variables, medians (min-max) for non-normally distributed variables, and frequencies (percentages) for nominal variables. Categorical variables were compared using χ^2 or Fisher's exact χ^2 tests. The success of TEE and 18F-FDG PET/CT alone in detecting lead endocarditis was evaluated with the McNemar test. Receiver operating characteristic (ROC) analysis was performed to compare TEE, 18F-FDG positron emission tomography (PET), and transthoracic echocardiography (TTE). The DeLong test for two associated ROC curves was used to evaluate statistical significance. Results were considered statistically significant for $P < 0.05$.

RESULTS

A total of 40 patients diagnosed with pocket infection and hospitalized with a preliminary diagnosis of lead endocarditis were included in our study. The mean age of the patients was 61.5 years, and 65% were male. Twelve patients had single-chamber implantable cardioverter-defibrillators (30%), 4 patients had dual-chamber implantable cardioverter-defibrillators (10%), 6 patients had single-chamber pacemakers (15%), 6 patients had dual-chamber pacemakers (15%). Twelve patients had biventricular-implantable cardioverter-defibrillators (ICD) (30%). Other baseline characteristics are summarized in Table 1.

Forty patients presented with signs of pocket infection (pain, erythema, swelling, discharge, wound dehiscence), 21 patients (52.5%) with fever and fatigue, and three patients (7.5%) with symptoms of decompensated heart failure. Six patients had a history of IE or had undergone multiple pocket revisions due to previous infections, and all six had previously received numerous antibiotic treatments. Blood cultures were positive in 15 patients (37.5%), with pathogens listed in Table 1. Methicillin-resistant coagulase-negative staphylococci (MRCoNS) (26.6%) and methicillin-sensitive *staphylococcus aureus* (MSSA) (26.6%) were the most commonly identified pathogens. Tissue culture was positive in 9 patients, with MSSA being the most

Table 1. Main characteristics of the study group

		Value
Sex, n (%)	Male	26 (65)
	Female	14 (35)
Age, mean (SD)		61.5 (13.5)
Device types, n (%)	Single-chamber ICD	12 (30)
	Single-chamber PM	6 (15)
	Dual-chamber PM	6 (15)
	BV-ICD	12 (30)
	DDD-ICD	4 (10)
Positive blood cultures, n (%)	Candida	1 (6.6)
	Enterococcus faecalis	1 (6.6)
	MRCoNS	4 (26.6)
	Polymicrobial	1 (6.6%)
	MSSA	4 (26.6)
	Streptococcus	2 (13.3)
	VRE	2 (13.3)
TEE positivity, n (%)	Mobile mass	12 (42.1)
	Immobilized mass	4 (17.3)
	Multiple masses	7 (30.4)
Positive tissue cultures n (%)	Candida	1 (11.1)
	MRCoNS	1 (11.1)
	Polymicrobial	1 (11.1)
	MSSA	4 (44.4)
	Streptococcus	1 (11.1)
	VRE	1 (11.1)
Lead cultures, n (%)	Negative	10 (25)
	Positive	2 (5)
	Absent	28 (70)
Initial modified Duke criteria, n (%)	Not lead endocarditis	2 (5)
	Possible lead endocarditis	21(52.5)
	Definite lead endocarditis	17 (42.5)
Follow-up, n (%)	Death	9 (22.5)
	Recurrent infection	3 (7.5)
	Recovery	28 (70)
Treatment, n (%)	Medical treatment	12 (30)
	Transvenous lead extraction	19 (47.5)
	Surgical treatment	3 (7.5)
	Pocket revision	6 (15)
18F-FDG PET, n (%)	No involvement	12 (30)
	Pocket involvement	10 (25)
	Lead and pocket involvement	16 (40)
	Systemic involvement	2 (5)

Abbreviations: 18F-FDG PET, positron emission tomography; BV-ICD, biventricular pacemaker and implantable cardioverter defibrillator; DDD-ICD, dual chamber pacemaker-defibrillator; ICD, implantable cardioverter-defibrillator; MRcONS, methicillin-resistant coagulase-negative staphylococci; MSSA, methycilline sensitive *Staphylococcus aureus*; PM, pacemaker; TEE, transesophageal echocardiography; VRE, vancomycin-resistant enterococcus

frequently isolated microorganism in 4 patients. Lead culture was positive in 2 patients. Eighteen patients (45%) were treated with medical or pocket revision during follow-up, so the lead culture was not obtained. Due to the study's retrospective nature, lead culture results of 10 patients (25%) could not be obtained from medical records. It was noted that eight of ten patients with negative lead cultures had a history of antibiotic use before transvenous lead extraction. TEE was completely negative in 17 patients (42.5%). Among the remaining patients, 12 (52.1%) had mobile masses on the lead, 4 (17.3%) had fixed masses, and 7 (30.4%) had multiple masses. According to the modified Duke criteria, two patients were classified as having no definitive lead endocarditis, 17 patients had definite lead endocarditis, and 21 patients had possible lead endocarditis. Among the 21 patients initially classified as having possible endocarditis, six were later diagnosed with definite lead endocarditis during follow-up.

All patients underwent 18F-FDG PET/CT. Eighty percent of the patients had received antibiotic treatment before the scan, and 35% had been on antibiotics for at least seven days. 18F-FDG PET/CT showed no uptake in 12 patients (30%). Among the remaining patients, 25% showed only involvement of the pocket, while systemic involvement was observed in 2 patients (Table 1). Devices and leads were removed entirely in 22 patients (55%), and lead cultures identified a pathogenic bacterium in 2 patients. Twelve patients (30%) received medical treatment, and 6 (15%) underwent pocket revision (Table 1). During follow-up, 23 patients were diagnosed with definite lead endocarditis, while 17 were considered free of lead endocarditis. The definitive diagnosis was based on reevaluation of the Duke score, which included pathological criteria (extracted lead cultures), alternative diagnoses, and new findings during follow-up.

Nine patients (20%) died during follow-up. Two patients underwent emergency surgery due to complications during transvenous lead extraction, leading to multiple organ failure and subsequent death. Four patients died due to progression of heart failure symptoms and rhythm disturbances during follow-up. One patient was diagnosed with leukemia and another with lung cancer. One patient died from a severe acute lung infection during the acute phase.

Among the 23 patients initially suspected of lead endocarditis based on TEE, follow-up confirmed the diagnosis in 14 cases. Of the 18 patients initially suspected of lead endocarditis based on 18F-FDG PET/CT, 17 were diagnosed with definite lead endocarditis during follow-up. Among the 22 patients with negative PET/CT scans, six had false negative results and were diagnosed with definite endocarditis (Table 2). Although neither imaging method alone was statistically sufficient to diagnose lead endocarditis, 18F-FDG PET/CT alone comes closer to diagnosing lead endocarditis.

The sensitivity, specificity, and positive/negative predictive values of 18F-FDG PET/CT, TEE, and TTE were calculated (Table 3). In a comparative analysis of diagnostic metrics between TEE and 18F-FDG PET/CT, as well as TEE and TTE (transthoracic echocardiography), the following results were obtained. For sensitivity, there was no statistically significant difference between TEE and 18F-FDG PET/CT ($P = 0.23$) or between TEE and TTE ($P = 1.0$). This strongly suggests that TEE's sensitivity is consistently comparable to 18 FDG PET/CT and TTE in detecting this condition. Regarding specificity, a statistically significant difference was observed between TEE and 18F-FDG PET/CT ($P < 0.001$), with 18F-FDG PET/CT showing higher specificity. Similarly,

Table 2. Performance of positron emission tomography and transesophageal echocardiography in diagnosing lead endocarditis when used alone as an imaging modality

			Definitive Diagnosis		
			Lead endocarditis (-) n (%)	Lead endocarditis (+) n (%)	*P*-value
Pre-diagnosis	TEE	Absent	8 (47.1)	9 (52.9)	1.000[a]
		Present	9 (39.1)	14 (60.9)	
	18F-FDG PET	Absent	16 (72.7)	6 (27.3)	0.125[a]
		Present	1 (5.6)	17 (94.4)	

[a]McNemar test used

Abbreviations: see Table 1

Table 3. Sensitivity and specificity of positron emission tomography, transesophageal echocardiography, and transthoracic echocardiography in detecting lead infection in patients with suspicion of lead endocarditis

	TEE (95% CI)	18F-FDG PET (95% CI)	*P*-value	TEE (95% CI)	TTE (95% CI)	*P*-value
Sensitivity	0.61 (0.41–0.78)	0.74 (0.54–0.87)	0.23	0.61 (0.41–0.78)	0.57 (0.37–0.74)	1.0
Specificity	0.47 (0.26–0.69)	0.94 (0.73–0.99)	<0.001	0.47 (0.26–0.69)	0.18 (0.06–0.41)	0.008
PPV	0.61 (0.41–0.78)	0.94 (0.74–0.99)	<0.001	0.61 (0.41–0.78)	0.48 (0.31–0.66)	0.37
NPV	0.47 (0.26–0.69)	0.73 (0.52–0.87)	0.04	0.47 (0.26–0.69)	0.23 (0.08–0.50)	0.03

Abbreviations: CI, confidence interval calculated; NPV, negative predictive value; PPV, positive predictive value; TTE, transthoracic echocardiography; other — see Table 1

a significant difference was found between TEE and TTE (P = 0.008), with TEE demonstrating higher specificity than TTE.

Significant differences were noted for the positive predictive value (PPV). The difference between TEE and 18F-FDG PET/CT was statistically significant (P <0.001), with 18F-FDG PET/CT exhibiting a higher PPV. However, no significant difference was found between TEE and TTE (P = 0.37). Lastly, the negative predictive value (NPV) also showed significant differences. The difference between TEE and 18F-FDG PET/CT was statistically significant (P = 0.04), with 18F-FDG PET/CT having a higher NPV. A significant difference was also observed between TEE and TTE (P = 0.03), with TEE showing a higher NPV than TTE. Our findings suggest that 18F-FDG PET/CT generally provides higher specificity and predictive values than TEE. However, TEE's sensitivity remains consistent across the methods compared, indicating its reliability in detecting this condition.

In the analysis of ROC curves comparing TEE and 18F-FDG PET/CT, the DeLong test for two correlated ROC curves was employed to assess the statistical significance of the difference in the area under the curve (AUC) between the two diagnostic methods (Figure 6). The results of the DeLong test indicated a significant difference in the AUC values between TEE and 18F-FDG PET/CT (P = 0.006). The AUC for TEE was estimated at 0.54, while the AUC for 18F-FDG PET/CT was significantly higher at 0.84. This significant difference, a key finding of our study, underscores the improved diagnostic accuracy of 18F-FDG PET/CT in diagnosing lead endocarditis compared with TEE. The same method was applied to compare TEE and TTE. The analysis demonstrated no statistically significant difference between the AUC of TEE and TTE (P = 0.20); this showed that the diagnostic performances of the two methods were statistically indistinguishable in diagnosing lead endocarditis.

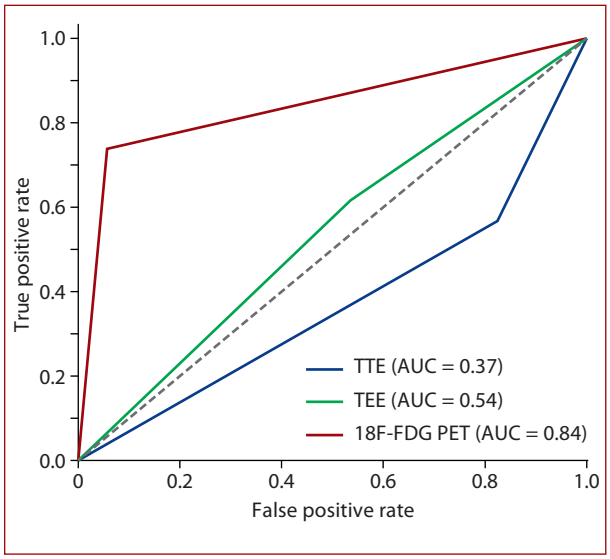

Figure 6. Receiver operating characteristic curves comparing positron emission tomography (18F-FDG PET), transesophageal echocardiography (TEE), and transthoracic echocardiography (TTE)

Abbreviation: AUC, area under the curve

DISCUSSION

Our investigation was a retrospective study comparing the diagnostic efficacy of TEE and 18F-FDG PET/CT in identifying lead endocarditis in patients previously diagnosed with pocket infection and monitored with a preliminary diagnosis of lead endocarditis. Our investigation demonstrated that 18F-FDG PET/CT outperformed TEE in diagnosing lead endocarditis. The findings of our study underscore the potential benefits of integrating 18F-FDG PET/CT into

the diagnostic protocol for patients with suspected lead endocarditis and intracardiac devices.

Our study evaluated the sensitivities and diagnostic performances of TTE and TEE, and no significant difference was found. In the survey by Klug et al. [14], TEE was superior (sensitivity 94%) to TTE (sensitivity 23%) in diagnosing lead endocarditis. We attribute this difference to the retrospective nature of our study as well as differences in the performing echocardiographic evaluations, changes in image quality, and the small population of our study.

Our study, which rigorously evaluated the diagnostic powers of 18F-FDG PET-CT and TEE in diagnosing lead endocarditis, led to a significant finding. It was demonstrated that these imaging techniques, when used alone, were insufficient in diagnosing lead endocarditis (P >0.05). This finding aligns with the survey conducted by Gomes et al. [15], where imaging techniques were compared head-to--head in 46 patients receiving TEE, multidetector computed tomography angiography (MDCTA), and 18F-FDG PET/CT. In patients with prostheses, the sensitivity was 75%, 75%, and 83%, respectively (100% when combined), while the specificity for all three methods was 86%. Our research findings highlight the need for a comprehensive and sequential evaluation when diagnosing endocarditis. It is crucial to remember that additional imaging methods should be used together to achieve accurate diagnosis when necessary. This approach, as our findings support, significantly enhances the effectiveness of the diagnosis.

Our results confirm those of the earlier single-center study conducted by Graziosi et al. [16], involving a cohort of 17 patients, with the notable distinction of our study's larger patient cohort and its superior statistical power. Despite the retrospective nature of our study, the reassessment of patients during follow-up allowed for a revision of their diagnoses. This showed a notable discrepancy, in a significant proportion of patients, between the initial diagnosis of lead endocarditis based on the Duke criteria and the final diagnosis, which highlights the considerable difficulty and frequent ambiguity associated with diagnosing lead endocarditis. Consequently, there is a heightened demand for advanced imaging modalities to overcome the over-reliance on TEE for lead endocarditis diagnosis. Within this context, 18F-FDG PET/CT emerges as a dependable imaging tool, as indicated by the findings of our study.

Our investigation illustrated the pivotal role this technique could play in diagnosis, particularly in patient cohorts characterized by inconclusive clinical and echocardiographic findings. The superiority of 18F-FDG PET/CT in diagnosis stems from its capacity to visualize the extracardiac segment of leads, differentiate between a thrombus and vegetation, diagnose septic emboli even in clinically asymptomatic scenarios, and facilitate early identification of lead involvement. Specifically, the inability of echocardiography to visualize the extracardiac segment of leads was highlighted in our study, wherein 18F-FDG PET/CT showed extracardiac lead involvement in two patients despite the absence of masses on TEE. Furthermore, in eight patients with TEE-detected masses but indistinguishable between vegetation and a thrombus, subsequent clinical follow-up and 18F-FDG PET/CT imaging confirmed the final diagnosis as thrombus, underscoring the superior discriminatory capability of 18F-FDG PET/CT in distinguishing between a thrombus and vegetation. Compared to other studies involving CIED patients diagnosed with infective endocarditis, the characteristics of our study population showed a lower average age and a lower rate of positive blood, tissue, and lead cultures [16, 17]. The predominance of negative cultures in our patient cohort was attributed to a significant proportion of patients receiving multiple antibiotics before diagnosis.

Additionally, our patient population exhibited a lower incidence of device revision than in other studies. In 5 patients, malignancy was diagnosed using 18F-FDG PET/CT, leading to early diagnosis and treatment initiation. This outcome was interpreted as a positive extracardiac finding of 18F-FDG PET/CT.

Some authors have advocated labeled leukocyte scintigraphy as an alternative diagnostic modality for identifying lead endocarditis. However, this approach is time-intensive [18]. Although labeled leukocyte scintigraphy exhibits somewhat greater specificity than 18F-FDG PET/CT, its sensitivity is notably lower [19]. Nevertheless, due to its high specificity, labeled leukocyte scintigraphy may prove valuable as a secondary imaging tool in patients with suspicious 18F-FDG PET/CT findings [20]. Due to its heightened sensitivity in detecting inflammatory and infectious activity, 18F-FDG PET/CT holds significant potential in diagnosing cardiovascular infections, with recent studies reporting promising outcomes in prosthetic valve and intracardiac device endocarditis [21–23]. For instance, Bensimhon et al. [24] observed that 18F-FDG PET/CT might be particularly beneficial in diagnosing device infections within pacemaker pockets. Graziosi reported that 18F-FDG PET/CT could enhance the diagnostic precision of the modified Duke criteria, especially in cases categorized as probable infective endocarditis within the subset of device infections [16].

In a study by Ploux et al. [17], augmented involvement was noted in patients with CIEDs where TEE yielded negative results, but a suspicion of device infection persisted, as evidenced by 18F-FDG PET/CT. In all such cases, the CIEDs were removed, with subsequent culture analysis showing microbial growth on the leads. Furthermore, differentiation between superficial infection and deep pocket infection was achieved. Pizzi et al. [25] demonstrated that including 18F-FDG PET/CT, mainly 18F-FDG PET/CT angiography, in the diagnostic workup of patients with suspicion of infective endocarditis can yield significant benefits. They found that the combination of the Duke criteria and 18F-FDG PET/CT, mainly when utilized in critical situations (such as two postoperative periprosthetic pseudoaneurysms, two post-pericardiotomy syndromes, and two cases of

pleuropericarditis), led to a substantial improvement in the diagnostic accuracy of IE.

Marciniak et al. [26] studied the sensitivity and specificity of 18F-FDG PET/CT for lead endocarditis and pocket infection. The sensitivity for detecting pocket infection was reported to be 91.7% with a specificity of 70%, but the sensitivity and specificity for detecting lead endocarditis were 100% and 47.1%, respectively [26]. This study found that 18F-FDG PET/CT is more useful in identifying pocket infection than lead endocarditis. In our investigation, the sensitivity for diagnosing lead endocarditis was 73.9%, and the specificity was 94.1%. In addition to the group with infection findings, Marciniak's study included a control group of individuals who did not have infection symptoms. However, in our investigation, all patients were diagnosed with a pocket infection, and there was no control group without infection results. We attribute the considerable variation in sensitivity and specificity between the two investigations to the different patient groups used.

Potential drawbacks of this diagnostic tool include its relatively high cost and limited availability. Its cost may be deemed high compared to TEE. However, 18F-FDG PET/CT scanning can be cost-effective if reserved for challenging diagnostic cases, such as patients with pacemakers and unknown fever. Confirming the diagnosis earlier can help avoid uncertainty in treatment and repeat testing while enabling prompt initiation of definitive therapy, thereby reducing hospital stays. Additionally, unnecessary and costly use of materials can be avoided in patients without infection.

Study limitations

This retrospective investigation necessitates validation through larger patient cohorts and prospective studies. The retrospective design showed deficiencies in interpreting imaging modalities (discordant TEE results across different interpreters) and obtaining culture outcomes (tissue, lead cultures). Most enrolled patients underwent multiple antibiotic therapies before culture sampling and 18F-FDG PET/CT imaging. This may have negatively impacted culture yields and decreased FDG uptake.

Our study was conducted with rigorous adherence to the qualification process for 18F-FDG PET/CT examination, which is a significant aspect of our research. One of the limitations we encountered was the small number of patients with a negative initial diagnosis (2 cases). This was primarily due to the high cost of that examination and the stringent eligibility criteria. In Türkiye, three physicians must approve the test, which is why it is performed only on patients with a high probability of endocarditis. As a result, the number of patients with a negative diagnosis in our study was low, which impacted the results. Furthermore, these challenges in 18F-FDG PET/CT imaging limited the sample size.

Confident investigators have underscored the importance of peripheral manifestations in IE and recommended the use of 18F-FDG PET/CT in this context. However, due to the retrospective nature of our study, detailed documentation of peripheral endocarditis findings were not included in patient records, precluding evaluation of this aspect of 18F-FDG PET/CT. Our study has elucidated the efficacy of 18F-FDG PET/CT in early tumor detection.

CONCLUSION

In patients with suspected lead endocarditis involving implantable cardiac electronic devices, 18F-FDG PET/CT surpasses TEE in establishing accurate diagnosis. Considering the impact of early diagnosis and treatment on mortality and morbidity in device infections, 18F-FDG PET/CT serves as a valuable diagnostic imaging modality for clinicians managing this complex scenario in patients with suspicion of lead endocarditis.

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